Review of Environmental Factors Affecting Hearing

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The major nongenetic causes of sensorineural hearing loss are exposure to noise, aging, ototoxic drugs, viral and bacterial infections, and interactions between these factors. Regarding exposure to continuous noise, the data base from laboratory and field studies indicates that a risk of hearing loss is present when noise levels exceed 75–80 dBA. As noise level, duration and number of exposures increase so does risk. The data base for other forms of noise (intermittent, impact) is not as established. Risk of hearing loss due to impulse noise increases as the peak SPL exceeds 145-155 dB and as the duration of the impulse, the number of impulses and the number of exposures increase. High-level acoustic impulses can cause severe, permanent hearing loss. Interaction between some steady-state noises and some acoustic impulses can be synergistic, producing extensive injuries to the organ of Corti. Noise can also interact synergistically with some aminoglycoside antibiotics to produce severe injuries to the inner ear. These antibiotics are also capable of producing hearing loss and indeed may do so in up to 55% of the one million persons who receive aminoglyociside antibiotics during the course of treatment for tuberculosis or severe gram-negative infections. Bacterial and viral infections may also produce mild to severe hearing loss. With the development of rubella vaccine and Rhogam, cytomegalovirus may have become the most common cause of congenital deafness. Aging is also a major cause of hearing loss. Exposure to occupational and environmental noise, certain diseases and life styles (diet, stress, drugs) may interact with the specific effects of aging. The result is moderate to severe hearing loss in a majority of older persons.

Introduction

This paper reviews major environmental factors which can affect hearing. Its focus is on those factors which produce injury to the cochlea and auditory nerve. Hearing losses arising from pathology of the cochlea and auditory nerve are referred to as sensorineural as opposed to conductive (external ear and middle ear) or central (CNS). The major causes of sensorineural hearing loss are exposure to noise, aging, drugs, genetic factors and a number of other factors including infections, head trauma, metabolic disorders and chemicals. Here, the major emphasis is on the effects of noise on hearing with minor attention given to aging, drugs, some of the

other agents and some of the major interactions which can occur.

Noise and Hearing

Exposure to noise can injure the inner ear and produce a sensorineural hearing loss. The injury and hearing loss can be temporary, permanent, or it can have temporary and permanent components. Since World War II considerable effort has been given to studies of noise-induced hearing loss. (1) These efforts include large-scale field studies of permanent effects in occupational settings (2-5), laboratory investigations of temporary effects with humans (6-8), and laboratory investigations with animals of temporary and permanent effects (9-11), including pathological anatomy and physiology (12, 13). Often the effects of noise on hearing are discussed in relation to the characteristics of the

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noise exposure. Three characteristics are discussed here: (1) continuous exposure to noise, (2) intermittent exposure and (3) impulse noise.

Continuous Exposure to Steady-State Noise

Laboratory Studies. Recent studies in human subjects (7, 14-17) of temporary changes in hearing (called temporary threshold shifts) produced by exposure to noise are consistent in several respects. Temporary threshold shifts (TTS) increase during the first 8-12 hr of a noise exposure and then reach an asymptote or plateau (Fig. 1). TTS's at asymptote increase about 1.7 dB per decibel increase in noise level above a critical level (7) as shown in Figure 2. The critical level of a noise centered at 4.0 kHz is 74 dB sound pressure level (SPL). According to the simple equation in Figure 2, then, the TTS is 0 dB when the critical level C is equal to the noise level. For other noises between 500 Hz and 4.0 kHz, TTS is computed by the same equation. That is, TTS increases about 1.7 dB per decibel increase in noise level above the critical level, which is dependent upon frequency (Fig. 3). The critical level is 74 dB at 4.0 kHz, 78 dB at 2.0 kHz, and 82 dB SPL at 1.0 and 0.5 kHz.

Also shown in Figure 3 are data from laboratory investigations with chinchillas and monkeys (7). Figure 3 shows that the relationship between temporary hearing loss and noise level described for humans is also accurate for chinchilla and monkey data when noise level is corrected by a constant (the critical level). Critical levels are frequency and species dependent. It appears, therefore, that the equations in Figure 3 are accurate for humans, chinchillas, some species of monkey and perhaps most mammals.

Several years ago it was hypothesized (14) that TTS at asymptote produced by a given sound is the upper limit of any permanent effect that can be produced by that sound regardless of the duration of scheduling of the exposure. This hypothesis is correct if TTS grows to an asymptote rather than an intermediate plateau. Research with chinchillas (20, 21) and monkeys (11) shows that the asymptote is maintained for as long as 90 (11, 20) or 108 days (21). Thus, if a noise produces a barely measurable TTS (5 dB) after about 12 hr of exposure, then it will not produce a permanent threshold shift in excess of 5 dB. The critical levels for TTS then define so-called "safe levels of noise," or "acoustic injury thresholds."

Critical levels are plotted in Figure 4, as well as the audibility and tolerance thresholds (22). Figure 4 can be taken as a range of likely acoustic injury and permanent hearing in humans. There are three
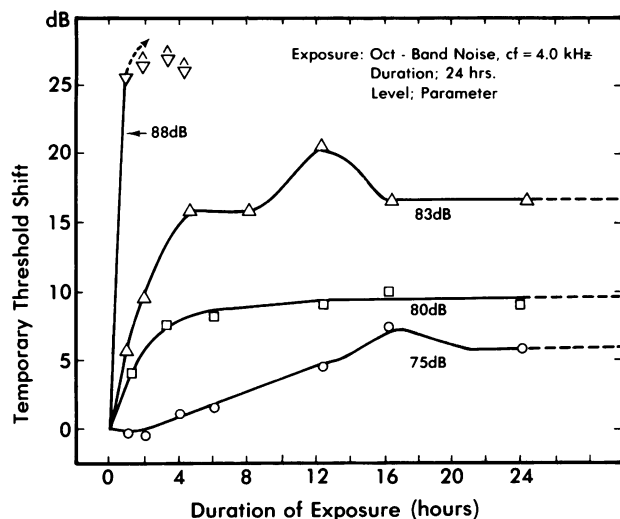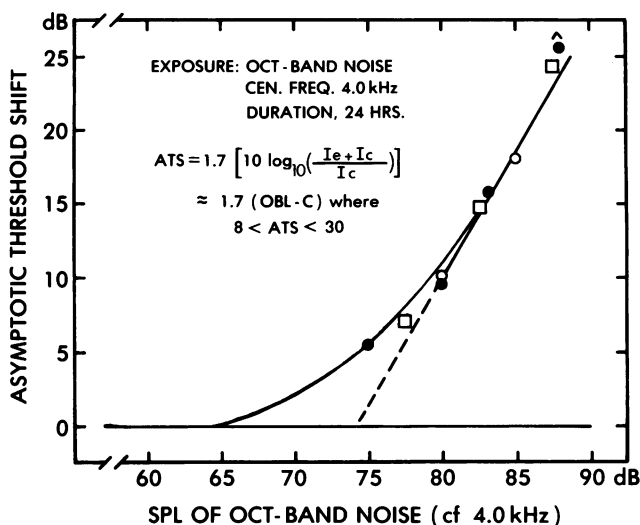

FIGURE 1. Temporary threshold shifts (TTS) as a function of the duration of exposure produced by an octave-band SPL of the noise centered at 4.0 kHz. The parameter is the octave-band SPL of the noise. Measurements of TTS were made about 4 min (TTS$_4$) after a subjects had been recovered from the noise. For the 88 dB exposure, some subjects had TTS's greater than 25 dB after 1-2 hr of the exposure. Therefore, the exposure was terminated (7).

FIGURE 2. Relation between TTS at asymptote and the octave-band SPL of a noise centered at 4.0 kHz (7). Critical levels (C) are estimated by a straight line extrapolation as shown by the dotted line.

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areas of interest in Figure 4. The region bounded by "injury thresholds" and the audibility curve represent sounds audible to humans which present no risk of injury to the ear regardless of the duration of exposure. The uppermost region (top of Fig. 4) represents sounds that present a high risk of injury. This region corresponds to so-called "discomfort thresholds" which are called discomfort (120 dB), tickle (125 dB), and pain (130 dB). Between the region of discomfort and the "injury thresholds" is the region where risk depends on the combined effects of level, duration, number of exposures, and individual differences. An increase in any of these exposure features increases risk, although the quantitative determination of the increased risk is the subject of much debate.

Individual differences in TTS and permanent threshold shifts (PTS) are not trivial (7, 23). Indeed, for a given noise exposure where the median TTS is 20 dB, individuals range from 5 to 35 dB. An explanation of individual differences, while not available currently, must surely include acoustic properties of the external middle, and inner ear, as well as details of the biological properties of the inner ear.

Field Studies: Permanent Effects. Noise-induced permanent threshold shifts (NIPTS) refers to permanent threshold shifts caused by exposure to industrial noise (corrected for age-related hearing loss). Most estimates of noise-induced permanent threshold shifts come from industrial field studies and are usually contaminated by a number of factors, including a chronic, temporary threshold shift component. The accuracy of these field studies is not universally accepted. Noise measurements, audiometric methods, control groups, and other factors are usually the focus of endless debate.

Regardless of these arguments, there are several excellent cross-sectional field studies in which the noise exposure was 8 hr per day (2-6, 24). A number of observations are common to these studies. At 4.0 kHz the median NIPTS increases rapidly during the first 10 years of exposure and then is asymptomatic or increases slightly between 20 and 50 years of exposure. The variability of NIPTS at 4.0 kHz as indicated by the semi-interquartile range reaches a maximum value of 12 to 20 dB after a few months or a few years and then decreases systematically to an asymptotic value of about 5 dB. It is quite possible that this asymptotic value of 5 dB is equal to the pre-exposure, semi-interquartile range (2). At 2.0 kHz the median NIPTS increases for about 30 years of exposure and then appears to
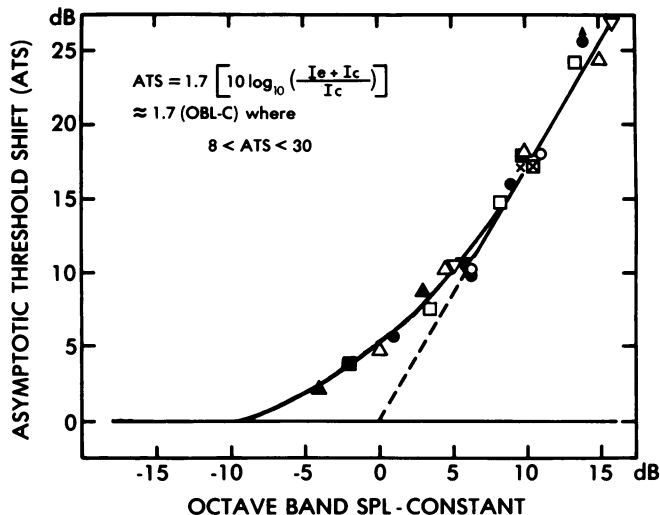

FIGURE 3. Relation between TTS at asymptote (at the test frequency of maximum shift) and the level of an octave-band noise minus a constant. Includes data from human, monkey, and chinchilla. The constant or critical level is dependent upon the center frequency of the noise and the species. For humans, the critical levels (C in the straight-line equation of Fig. 3) is 82 dB SPL at 0.5 and 1.0 kHz, 78 dB at 2.0 kHz and 74 dB at 4.0 kHz. For a wide-band noise, C is 78 dBA. For additional details see Mills et al. (7).
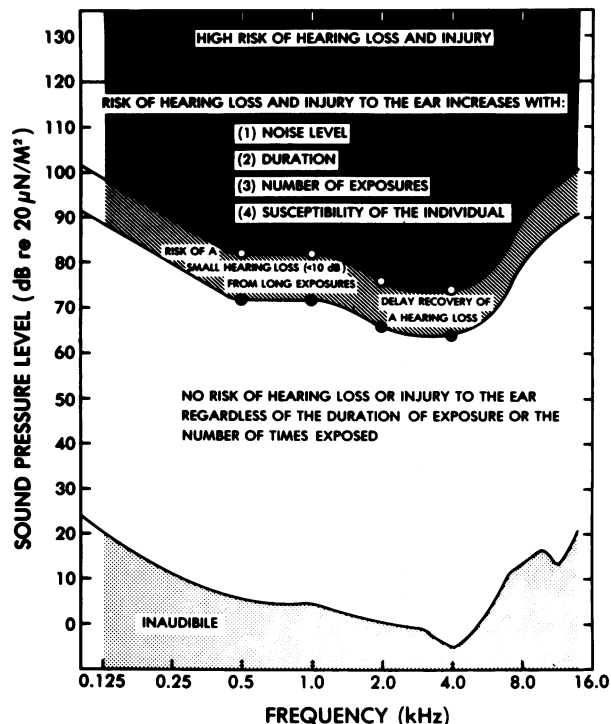

FIGURE 4. Range of human audibility categorized with respect to the likelihood of acoustic injury of the ear and noise-induced hearing loss (26).

reach an asymptote. Variability of NIPTS reaches a maximum after 20 years of exposure, remains constant between about 20 and 30 years of exposure, and then decreases and reaches an asymptotic value of about 5-7 dB after about 40 years of exposure.

The major difference between variability at 4.0 kHz and at 2.0 kHz appears to be in the temporal domain. That is, maximum semi-interquartile range at 2.0 kHz (16 to 17 dB) is nearly equal to the maximum at 4.0 kHz; however, the maximum at 2.0 kHz is reached after about 20 years of exposure, whereas the maximum at 4.0 kHz is reached after less than 5 years of exposure.

Of some significance is the possible relationship between the median value of NIPTS and the variability of NIPTS as indicated by the semi-interquartile range. The variability of NIPTS always reaches a maximum several years before the median NIPTS and at a time when the rate of change of the median is the greatest (or nearly so). Similarly, variability of NIPTS is smallest when the median NIPTS is largest and the rate of change of the median in minimal. In other words, the relation between the variability of NIPTS and median NIPTS is nearly identical to that observed in many dynamic systems where the variability of response varies directly with the rate of change of response. A complete explanation of individual differences is likely to require consideration of many acoustic, physiological and anatomical variables, as well as many non-auditory variables, such as diet and drugs.

Laboratory and Field Studies. Many of the laboratory studies of TTS have arisen from an interest in the problem of NIPTS. We make no effort to explain all the possible correlations between TTS and NIPTS. Rather, the effort here is to show the correspondence between results from laboratory studies of TTS and from field studies of NIPTS. Figure 5 shows threshold shifts plotted as a function of noise level, where noise level is corrected by subtracting a constant. Threshold shifts are TTS's from Figure 3 as well as additional TTS data from chinchillas (*10, 18, 19*). Other threshold shifts in Figure 5 are NIPTS's from field studies summarized by von Gierke and Johnson (*25*). Figure 5 has several features worthy of comment. One is that the empirical equations developed nearly 10 years ago for TTS in chinchillas can accurately describe TTS in man and monkeys, NIPTS (50th percentile) at 4.0 kHz after 10 years of exposure, and NIPTS (90th percentile) at 4.0 kHz after 10 or 30-40 years of exposure. The only correction required is the subtracted constant. That is, to equate the 90th percentile with the 50th percentile in NIPTS at 4.0 kHz after 10 years of exposure, noise level should be changed by 7.5 dB. To equate TTS with NIPTS
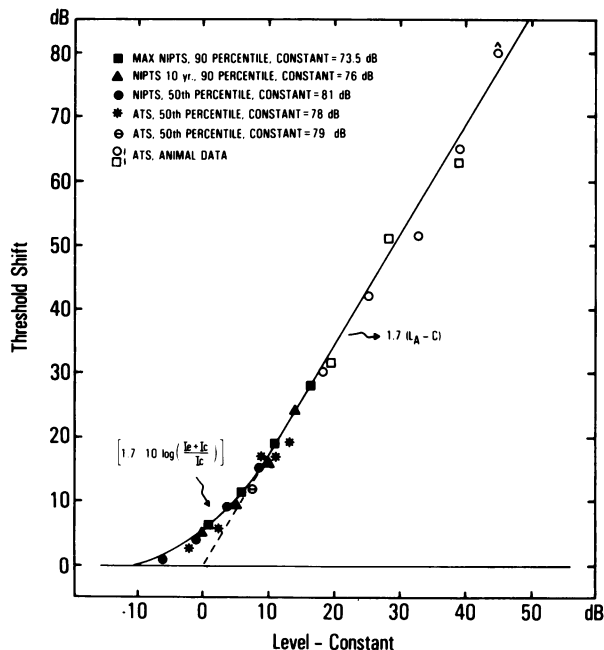

FIGURE 5. Relation between noise level and hearing loss. Data are from Figure 3 and field studies of noise-induced permanent threshold shifts in industrial workers (*25*). This figure links field studies with humans and laboratory studies with humans and animals (*58*).

(50th percentile, 10 year) noise level should be changed by 3 dB.

The data shown in Figure 5 are supported also in a recent study (*24*) which shows an NIPTS of about 15 dB at 4.0 kHz after about 10 years of exposure to a noise with an A-weighted sound pressure level of 89 dB. TTS data from Figure 5 predict that NIPTS at 3.5-4.0 kHz would be less than 18.7 dB, and NIPTS data in figure 5 predict an NIPTS of 13 to 14 dB. The agreement between these data (*24, 25*) and the different sets of NIPTS data shown in Figure 5 is striking. The predictions from TTS data can be considered excellent as well, particularly since the "error" of 3.7 dB is in the proper direction.

Currently, many persons are debating the merits of an 85 dBA noise for 8 hr versus 90 dBA for 8 hr. It is our belief that the audiometric effects of such exposure can be predicted from the data on Figure 5. Indeed, in our opinion the "85 dBA versus 90 dBA" controversy is clearly a social-economic-political issue which necessarily must be resolved by those who make social-economic-political decisions. In other words, data from additional experiments are not the solution to the 85 dBA versus 90 dBA controversy.

Mechanism of TTS and PTS. The mechanisms

of TTS and PTS are not known. For moderate level exposure one is inclined to think of a metabolic or biochemical bases, including the depletion of energy stores, assembly of cell membranes, effects on proteins and lipids of the cochlea, mechanically induced changes in the shape of the tectorial membrane, and vaso-constriction within the cochlea. For high-level exposure one is inclined toward a purely mechanical basis where in the input to the cochlea is intense enough to drive the basilar membrane beyond its normal range of displacement. The attached structures (organ of Corti) and unattached structures (Reissner's membrane) are thus "ruptured." The determination of the mechanism(s) of acoustic injury probably awaits the determination of the transduction mechanism of the cochlea, and basic information on the biochemistry of the cochlea, including action filaments of the stereocilia.

Noncontinuous Exposure

Whereas the data base is massive for the effects of continuous exposure to steady-state noise, the data base is less impressive for intermittent exposure to steady-state noise or intermittent exposure to noises with fluctuating levels. It is difficult to find occupational settings where the noise exposure can be clearly defined and measured accurately, and where there are a large number of employees who are employed for 20-40 years. Similarly, laboratory investigations must use humans (TTS) or animals, and the researcher is confronted with an almost endless list of variables. Moreover, because of regulatory efforts and their need for simplicity, there has been a fascination with the idea of a single-number correction factor. For example, one approach has been to equate noises with greatly varying temporal properties in terms of equal energy, equal pressure or compromises on equal energy or equal pressure. Thus, a steady-state noise exposure for 8 hr with a sound pressure level of 90 dBA is assumed to be equal to an exposure of 4 hr at 96 dBA, 95 dBA, 94 dBA, or 93 dBA. In other words, there is great debate and confusion regarding the exchange of the intensity of the noise and the duration of the exposure. A compromise is the "5 dB rule" currently used by OSHA and the Department of Labor.

Our thesis is that a single-number correction factor which specifies a time-intensity trade-off in NIPTS or TTS is doomed to be grossly incorrect at worst, or, at best, to have a very restricted range of application. This thesis is based on available literature and the results of a current project in our laboratory. Our results (26, 27) indicate that a number to describe time/intensity trading ranges from 0 dB to as large as 8 dB. The situation is complicated in part because of the ability of the ear to use quiet periods to recover from the noisy periods. In other words, rest periods as short as a few seconds may be useful in protecting the ear, particularly in those conditions where the noise is present for only a few minutes. It is perhaps because of these quiet periods that rock musicians and others similarly exposed do not have large hearing losses.

Impulse Noise

The acoustic impulses produced by handguns and rifles are the cause of mild-to-severe sensorineural hearing losses (28). High-frequency hearing losses are typical of persons exposed to acoustic impulses with peak sound pressure levels in excess of about 145-155 dB SPL. Among hunters and military personnel, PTS is usually largest in the left ear. The right ear (right handed shooter) receives less acoustic energy than the left because of the head-shadow effect.

The risk of NIPTS from acoustic impulses generally increases as the number of impulses increases, as the peak SPL of the impulses increases, and as the duration of each impulse increases. Also, specification of impulse duration is complicated, but apparently a critical factor. Detailed discussions of impulse noise and its effects on hearing are given elsewhere (29).

It is worth noting that laboratory investigations with human subjects are very difficult to do without placing the subjects at risk. An impulse at a given level and repetition rate may produce very little in the way of measurable effects. However, 10 dB increase in level may produce an unusually large shift. In other words, the range of levels available to an experimenter is small, and individual differences are large. It is disconcerting to note many anecdotal and clinical reports which show severe hearing loss after exposure to one impulse (acoustic trauma) or to a series of impulses (29). In fact, there are many reports documenting that acoustic impulses which had been innocuous on many previous occasions produce severe unilateral or bilateral PTS on a subsequent occasion.

The nature of the hearing loss produced by acoustic impulses is probably different from the nature of the hearing loss caused by continuous exposures to steady-state noise at moderate levels (for example, 90 dBA). That is, the displacement of the basilar membrane by an intense acoustic impulse may be sufficient to produce "ripping and tearing" effects. Purely mechanical injuries may be produced by acoustic impulses, whereas injuries produced by lower-level acoustic signals may be caused by metabolic, biochemical, or vascular effects.

Interactions

One acoustic event which is innocuous to the cochlea by itself can interact with another innocuous acoustic event to produce a large injury to the organ of Corti. The most dramatic example of "acoustic synergism" is the combined effects of noise and acoustic impulses (30). For example, a 157 dB impulse by itself or a noise of 95 dB produced no PTS or injury to the sensory cells, but the combined effect of the impulse and the noise was devastating. PTS ranged from 5 dB at 250 Hz, to 50 dB at 2.0 kHz and to 35 dB at 8.0 kHz. Outer hair cells were totally destroyed over a 7 mm region of the basilar membrane. Injury to inner hair cells was nearly as severe. These results have been documented in a series of experiments using other levels of impulses and continuous noise. There are, no doubt, other interactions between acoustic events which can either increase or decrease the risk of hearing loss. For example, a noise presented before an acoustic impulse can contract the stapedius muscle (acoustic reflex) (31). The impulse is then attenuated in the middle ear and the inner ear is thus protected. In the absence of the noise, the impulse travels through the middle ear before the reflex is activated (reflex latency 10 msec).

Exposure to Noise and Auditory Perceptual Deficits

Studies of auditory discrimination and reading skills of children living near freeways suggest deleterious environmental effects (32, 33). In this study, where noise levels inside apartments ranged from 55 dBA to 75 dBA, the performance of 2nd to 5th grade children on standardized speech discrimination and reading tests were correlated (0.48, 0.53) with noise levels for children who had resided in the apartment complex for at least four years. Substantially more data are required to clarify all of the issues involved. Moreover, it remains unclear whether noise-related deficits in speech discrimination and reading are temporary and will be overcome by maturation and schooling, or are permanent. These data (32) may be the first to indicate strongly that the development of important skills such as listening and reading is being affected by environmental noise.

Aging

While it may or may not be legitimate to include aging as an environmental factor, the loss of hearing associated with aging is a major problem. It will become far more significant in the next decades;

therefore, it is difficult to ignore in a discussion of causes of hearing loss.

The loss of hearing associated with aging is called presbyacusis. Presbyacusis has been subdivided into four categories: sensory, where the major pathology is at the outer and inner hair cells; neural, where the major pathology is indicated by large losses of spiral ganglion cells (cell body of Nerve VIII); metabolic, where major pathology is at the stria vascularis of the cochlea; and mechanical, where it is postulated that the elasticity or compliance of the basilar membrane and other structures is reduced. Of course, the CNS does not escape the effects of aging, nor does the sensitivity of other sensory systems, including gustatory, olfactory and ocular (34).

Auditory sensitivity for pure tones (audiogram) and other auditory behavior are affected in a manner that reflects to some extent the major pathology. For example, sensory and mechanical types of presbyacusis usually show moderate to severe losses in the high frequencies. In neural presbyacusis the audiogram may be normal or nearly so until greater than 50-80% of the spiral ganglion cells are missing. In cases of metabolic presbyacusis the hearing loss is moderate and affects all frequencies nearly equally.

While the quantitative facts of presbyacusis are important to clinical diagnosis and to patient management, they have significance as well to the problem of noise-induced hearing loss. That is, how much of a person's hearing loss is due to noises of everyday living (sociocusis); to previous infections, blows to the head, drugs, etc. (nosoacusis)? How do all of these causes of hearing loss interact and what is the nature of the interaction?

It is assumed that the effects of presbyacusis add linearly to the effects of occupational noise exposure. Moreover, presbyacusic control groups and occupational noise groups are assumed to have equal amounts of sociocusis and nosoacusis. Of course, these are extremely convenient assumptions which are necessary to permit the calculation of NIPTS. For group averages they may even have some accuracy. However, on an individual basis, gross errors probably occur. It is difficult to imagine that the additivity rules of neural presbyacusis is quantitatively identical to the additivity in mechanical presbyacusis.

The concept of presbyacusis has been altered by the results of studies completed in other cultures. Perhaps the most often quoted example is that of the Mabaan tribe of Africa (35). In this extremely quiet culture, the auditory thresholds of 80 or 90-year-old persons were approximately equal to those of 20-year-old persons in industrialized cities of North America and Europe. While some persons

were quick to note the absence of noise, the authors pointed to the absence of cardiovascular disease, the absence of meat in the diet, the climate, the absence of stress, and the absence of peptic ulcers. It was concluded that hearing loss in old age is attributable not just to the effects of noise, drugs and aging, but to the cumulative effects of these factors plus diet and stress-lifestyle factors. It is equally important to note that in Mabaans who had moved to Egypt, there was an unusually high incidence (for Mabaans) of hearing loss, cardiovascular disease and peptic ulcers. In other words, auditory skills are affected directly by definitive agents such as noise and drugs, and by lifestyle as well.

Ototoxic Drugs and Viral Infections

Ototoxicity from aminoglycoside antibiotics is well known (36-40). The aminoglycosides have a 2-decoxystreptamine as a central component. All are produced by the Streptomyces genus except the gentamycins, which are produced by a strain of *Micromonospora purpurea*. These antiboitics, which include kanamycin, gentamycin, neomycin, tobramycin, amikacin, sisomicin, netilmicin, and others, are bacteriocidal because they bind to proteins on the 30 S segment of the ribosome.

Aminglycoside antiboitics are indicated in the treatment of tuberculosis and serious gram negative infections with such bacteria as *E. coli*, Klebsiella, Proteus, *Pseudomonas aeruginosa*, and Serratia, for example (36-40). Aminoglycoside antibiotics are used to treat at least one million people in the U.S. annually (40), and perhaps as many as four million (41).

Ototoxicity from aminoglycoside antibiotics may be cochleotoxic and vestibulotoxic. Tobramycin and amikacin are considered more cochleotoxic, whereas streptomycin and gentamycin are considered more vestibulotoxic. The incidence of ototoxicity varies from 2% to 25% and perhaps as high as 55% (40, 41). In a prospective study of 38 courses of therapy in 113 patients (40), some significant associations with ototoxicity included high temperature elevated hematocrit, high creatinine clearance, poor condition of the patient and duration of therapy greater then 10 days. Serum levels, age, prior noise exposure and use of their ototoxic drugs were not found to be significantly correlated with the incidence of aminoglycoside ototoxicity.

Cochlear toxicity from aminoglycoside antibiotics affects the inner row of outer hair cells first, followed by the outer rows of hair cells, then by the inner hair cells (40). The pathology has also been localized to the stria vascularis, spiral ligament, and spiral prominence. Several theories of the mech-

anism of damage have been proposed, including direct damage to the hair cells and disruption of the metabolism in the stria vascularis and spiral ligament, which leads to changes in cationic differences of the perilymph and endolymph (40). The mechanism of vestibular damage remains poorly defined.

Hearing loss produced by aminoglycoside antibiotics ranges from minimal to severe. It usually starts at high frequencies and progresses to low frequencies. Efforts at early detection of otoxicity are sometimes only marginally successful at restricting the magnitude of the hearing loss. By the time reliable changes in the audiogram are detected, the degenerative process is underway and may continue for weeks or months after termination of the antibiotic.

Noise and some types of aminoglycosides interact synergistically in a most dramatic fashion (41). Noise exposure that produced minimal injury to the organ of Corti, and kanamycin administrations that also produced minimal injury acted synergistically and destroyed nearly 80% of the outer hair cells (41). No doubt, the aminoglycosides also interact with agents other than noise; however, the almost endless list of possible interactions is not well documented.

Whereas aminoglycosides can have severe effects on the organ of Corti and produce severe hearing loss, large doses of salicylates apparently produce only small (10-12 dB) hearing loss that is totally recoverable when the therapy is terminated. Moreover, there is little, if any, interaction between salicylates and noises of the impulse or steady-state variety (44, 45).

A large number of viral infections have been associated with sensorineural hearing losses. Rubella and mumps are the classic examples. Hearing loss with mumps is usually unilateral, whereas the loss with rubella is bilateral. In both cases the temporal bone pathology includes extensive degneration of sensory cells, stria vascularis, and tectorial membrane as well as the nerve supply (46, 47). Recently, the cytomegalovirus (CMV), a member of the herpes group, has been isolated from the perilymph and has been shown to cause congenital deafness. Inclusion-bearing cells have been observed in the epithelium of the utricular and saccular macula, Riessner's membrane and stria vascularis (54). It may possibly cause progressive hearing loss which starts at about two years of age (48-51). Severe middle ear infections are also associated with CMV (51).

Other viruses which have been implicated in both the gradual and sudden onset of sensorineural hearing loss include influenza, adenovirus, and herpes hominis (52, 53). Most viral infections of the inner

ear are described as "endolymphatic labyrinthitis" with a pathology consisting of degeneration of the stria vascularis, organ of Corti, and tectorial membrane.

A large number of other factors are assumed to affect hearing. These include a long list of chemicals (55) and bacterial infections (56), as well as over 40 genetic and metabolic syndromes (57).

General Comments

It is our belief that the state of the art concerning the causes of hearing loss has advanced in the past twenty years and restrictions in the discussion of hearing and hearing loss often occur because of a lack of basic information. The study of the biochemistry of hearing is in its infancy, neural transmitters in the cochlea are not discovered, the transducer mechanism of the cochlea is still debated, and details of the neural "wiring" diagram of the cochlea are unresolved. Similarly, the function of the outer hair cells and the efferent auditory system is not agreed upon. When these basic issues are resolved, there ought to be significant gains made in the detection, diagnosis and treatment of sensorineural hearing loss.

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